Artificial Disc Replacement
Health Technology Assessment

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Background

Degenerative disc disease (DDD) is defined in terms of anatomical, biomechanical, radiological and clinical change in the lumbar or cervical spine. Symptoms include pain exacerbated by activities that increase loads on the intervertebral discs.

Patients with severe pain may undergo conservative treatment or surgery. Discectomy usually addresses direct nerve root compression, but is not usually indicated for discogenic pain. (Ray 2002) The traditional surgery option of fusion has been shown to lead to donor site morbidity, pseudoarthrosis, and degeneration at the adjacent intervertebral disc.

The newer surgical option of artificial disc replacement is also intended to address pain due to DDD. Sagittal motion data suggests that the disc replacement may preserve motion as well as increase or restore motion. Researchers suggest that maintaining motion may protect against future degeneration at adjacent levels. (Delamarter 2003)

Two categories of artificial disc replacement devices are currently in use: intervertebral prostheses and disc nucleus replacements. Nucleus replacement products are designed for moderate degeneration while intervertebral prostheses are indicated for more severe degeneration. In contrast to intervertebral prostheses, nucleus replacement preserves the existing structures, which include the annulus, endplates, and ligaments. (Shim 2003) (MAS 2004)

Bertagnoli has suggested the following criteria to determine candidacy for intervertebral disc replacement.

Bertagnoli Criteria for Total Disc Replacement

Indications	Disc levels	Accompanying features
Prime	Single level	>4 mm remaining disc height No OA changes to facet joints No adjacent level degeneration Intact posterior elements
Good	Single level Double level	> 4 mm remaining disc height No primary OA changes to facet joints Minimum degeneration of adjacent discs Minimum posterior segment instability

Borderline	Single level Double level Triple level	< 4 mm remaining disc height Primary OA changes to facet joints Minimum adjacent level degeneration Minimum posterior segment instability Adjacent to fusions
Poor	Single level Double level Triple level	Gross degeneration of the spine Secondary OA changes to the facet joints < 4 mm disc height remaining at the same adjacent levels Posterior segment instability

Regulatory Status

Although new in the United States, disc prostheses are approved for use in Europe, Asia, and Canada.

I. Intervertebral prostheses

Intervertebral prostheses products for use in the lumbar region include SB Charité III and ProDisc II.

At this time, the Food and Drug Administration (FDA) has only approved the Charité III from DePuy Spine, Inc. Charité III was approved for use in patients who have DDD at one level in the lumbar spine (from L4-S1) and who have had no relief from low back pain after at least six months of non-surgical treatment.

The FDA is requiring DePuy Spine to conduct a post-approval study to assess the product's long-term safety and effectiveness, including its impact on other discs and on the bony structures on the back of the spine. (FDA 2004)

The ProDisc II is undergoing study through the FDA's Investigational Device Exemption (IDE) program and is awaiting approval.

II. Disc nucleus replacement

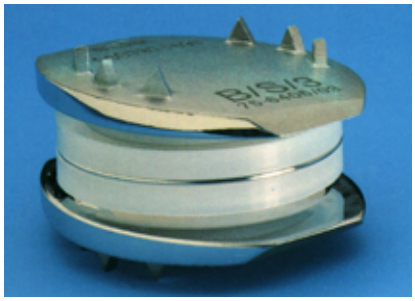
PDN, one disc nucleus replacement device, is undergoing study through the FDA's Investigational Device Exemption (IDE) program and is awaiting approval.

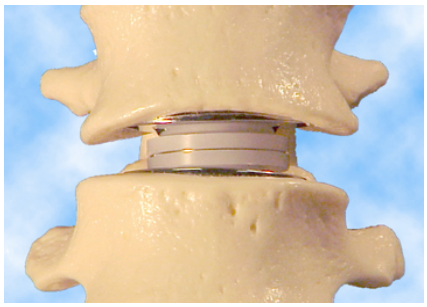
Search strategy

This assessment was conducted in order to evaluate the current literature on artificial disc replacement. Using the terms "disc replacement" and "artificial disc", PubMed and the Centre for Reviews and Dissemination databases were searched for English language articles published through July 2004. Only prospective trials with human subjects were included. Reference lists from identified articles were also hand searched.

Intervertebral Disc Prostheses: Charité III Prosthetic

SB Charité III has several features:
1. a high molecular weight polyethylene cast CoCrMoy alloy articulating bearing surface
2. a mobile bearing design
3. TiCaP porous ingrowth surface
4. vertebral body bone stock preservation (McAfee and Fedder 2003)





From http://www.spine-surgery.com/SSPSC/Artificial%20Disc%20Replacement/discreplacementsurgery2.htm

I. Studies from the Food and Drug Administration (FDA) Investigational Device Exemption (IDE) program

The FDA released that 205 patients who received the Charité III disc were compared to 99 patients who received fusion. The study showed that two years after surgery, patients in the two groups had similar outcomes and rates of adverse events. In addition, the study showed no statistically significant relationship between motion at the level where the disc was implanted and the patient's relief from pain. (FDA 2004)

a. McAfee conducted a randomized trial as part of the FDA IDE process. (McAfee and Fedder 2003)

The randomization design allowed for a two-third chance for disc replacement and a one-third chance for anterior interbody BAK interbody fusion using autograft. All surgeries were conducted with an anterior retroperitoneal approach.

Outcomes were independently assessed with the Oswestry scale and a pain VAS.

Patients were selected according to the following criteria.

Inclusion	Exclusion
• Between 18 and 60 years old • Symptomatic degenerative disc disease[1] or lumbar spondylosis documented by CT or MRI • Provocative discogram • Only single intervertebral level disc disease at L4-L5 or L5-S1 • Failed 6 months of conservative therapy[2]	• Radicular pain • Neurogenic claudication • Previous fusion • Osteopenia • Nerve root compression • Straight leg tests that produced pain below the knee • Spinal fracture • Spondylolysis • Spondylolisthesis • Scoliosis • Tumor • Facet joint arthrosis, >1 SD over normal body weight • Bilateral facetectomies

Study Population: 41 patients underwent disc replacement, and 19 patients underwent BAK as part of the control group. Patients had a mean age of 40.3 years. 19 surgeries were conducted at the L4-L5 level, and 41 surgeries occurred at the L5-S1 level.

Results: Although the trial used a randomized design, the FDA required reporting of both treatment groups together.

Follow-up ranged from 1 to 3 years, and no patients were lost-to-follow-up.

Average surgery length for both groups was 88.4 minutes, and estimated blood loss was 289.5 ml. The average hospital stay was 3.03 days.

Aggregate VAS and Oswestry scores for SB Charité and BAK

	Preoperative	Postoperative
VAS	73.5	30.4
Oswestry	50.0	25.0

[1] Degenerative disc disease is defined as discogenic back pain with degeneration of the disc as confirmed by history and radiographic studies with one or more of the following factors:

- contained herniated nucleus pulposus,
- paucity of facet joint degeneration changes,
- decrease of intervertebral disc height of at least 4 mm, or
- scarring/thickening of annulus fibrosis with osteophytes indicating osteoarthritis.

[2] Conservative therapy includes physical therapy, facet joint injections, epidural steroids, acupuncture, back school, behavior modification, ultrasound, anti-inflammatory medications, muscle relaxants, orthotics

b. In 2003, Blumenthal et al published data from one center of the multi-center, randomized trial submitted to the FDA. (Blumenthal and Ohnmeiss 2003) (Hochschuler 2002)

In addition to the inclusion and exclusion criteria of the McAfee study, patients in the Blumenthal study had baseline Oswestry scores of at least 30 and baseline VAS scores of at least 40.

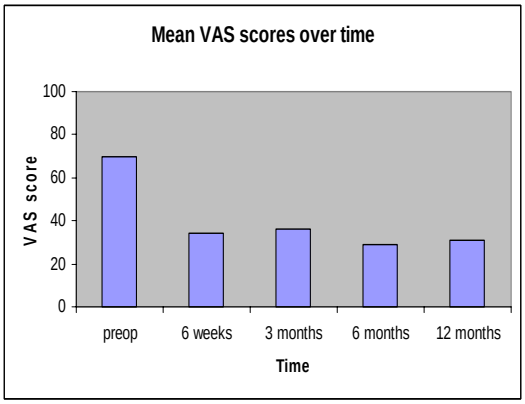
Data were collected at 6 weeks, 3 months, 6 months, and 12 months.

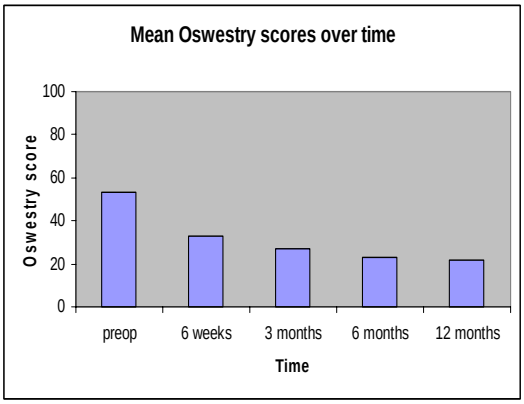
Study Population: The case series describes a consecutive series of 57 patients. Surgeries occurred at the L5-S1 level for 45 patients and at the L4-L5 level for 12 patients.

Results:

Mean operative time and blood loss

	L4-L5 (n=12)	L5-S1 (n=45)	All levels (n=57)
Operating time (min)	95.2	74.4	78.7
Blood loss (mL)	265.9	101.4	134.3





II. Published, Prospective Case Series Studies

a. Kim et al conducted a prospective study to evaluate the efficacy of disc replacement for juxtafusional degeneration following spinal fusion. (Kim and Lee 2003)

Following operation, standing and dynamic radiographs were scheduled at 1 day, 1 month, 3 months, 6 months, and every 6 months thereafter. Outcomes were also measured with the Oswestry and MacNab scales.

The study defined failure as any patient subject to reoperation due to implant or technical failure or with significant operation related complications.

Study Population: Subjects were included in the study if their neurologic disturbance and/or severe back pain compromised activities of daily living (ADL). In addition, patients did not respond to more than 6 months of conservative treatments.

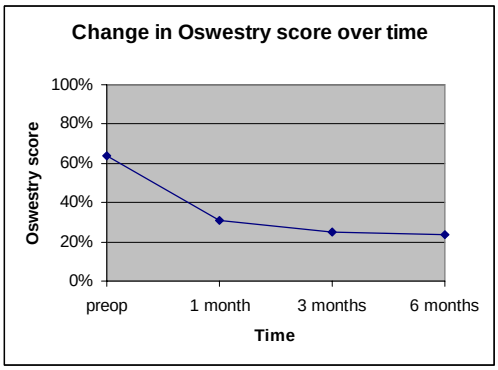
Subjects were excluded due to segment of interest higher than L1-L2, fractured vertebral body, facet joint degeneration, posterior element incompetence resulting in ante or retrolisthesis, spinal misalignment, disc space tilting and/or wedging in the coronal and sagittal planes, or negative discography.

Of the 11 subjects who received disc replacement, 5 subjects were followed for more than 6 months. Disc replacement occurred at 6 levels (L1-L2, L3-L4 for 2 patients, L5-S1, and L3-L4-L5).

Subjects had a mean age of 50.3 years. The average time between fusion and disc replacement was 4.9 years.

Results: Mean operating time was 180 minutes with a mean blood loss of 300 ml.

All 4 patients with neurologic compromise showed improvement of symptoms.



MacNab criteria was excellent in 3 subjects and good in 2 subjects at 6 months.

b. Sott et al assessed 14 patients (mean age 48 years) on pain, neurological symptoms, and disability. Patients were excluded due to spinal stenosis or significant nerve root compression. (Sott and Harrison 2000)

15 prostheses were implanted into 14 patients at levels L4-L5 (n=9), L3-L4 (n=3), and L5-S1 (n=2).

After an average of 48 months, 4 patients were unable to attend the last follow-up clinic, but were assessed over the telephone.

Results: Patients were stratified by age and were shown to experience the following outcomes using the Stauffer and Coventry scale[3].

	Good	Fair	Poor
< 45 years (n=7)	5	1	1
> 45 years (n=7)	5	1	1

Seven of the 10 patient with good results had taken no time off work preoperatively and returned to their jobs within 2 months of surgery. A total of 12 patients returned to work.

c. Zeegers prospectively monitored for two years the outcomes of 50 patients (75 prostheses) with lumbar discopathies. 18 patients were implanted at 2 levels, and 3 patients were implanted at 3 levels. (Zeegers and Bohnen 1999)

Subjects had a mean age of 43 years and a mean duration of back pain of 10 years. 27 patients had undergone previous surgery.

Results: Four patients were lost to follow-up.

70% of patients (32/46) had a positive clinical result. 65% of patients (30/46) showed improvement of low back pain, and 64% (27/42) reported improvement in leg pain. Of the 34 patients who used analgesics, 15 were able to decrease intake.

Patients without previous surgery and age under 45 demonstrated significantly better clinical results at 1 year.

81% of subjects (35/43) returned to some work, and 43% returned to their original work

12 patients out of 50 required reoperation.

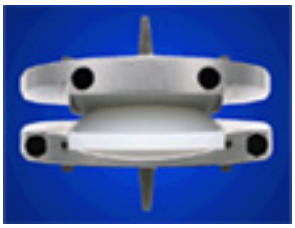
[3] Stauffer and Coventry scale

	Pain relief	Return to work	Physical restriction	Use of analgesics
Good	76-100%	Yes	No or slight	No
Fair	26-75%	Yes, with limitation	Yes, limited activities	Frequent (mild)
Poor	<25%	No, disabled	Yes, greatly limited	Regular (strong)

Intervertebral Disc Prostheses: Prodisc II

The ProDisc II prosthesis design is based on spherical articulation, with a convex polyethylene component articulating with a concave metal component. The metal endplates are made of a cobalt chromium molybdenum alloy.

The endplates are inserted in a collapsed form into the evacuated disc space. Then the insert is implanted with the convex bearing surface snapping into the inferior endplate. Spikes on each endplate as well as a large central keel anchor the disc and control rotation.



From http://www.spine-dr.com/site/surgery/surgery_total_disc.html

There are two endplate sizes, three heights of the polyethylene component, and 2 lordosis angles. (Zigler 2003)

I. Data from the Food and Drug Administration's Investigational Device Exemption process

   a. Delamarter provided comparative and descriptive analyses of the first 53 randomized patients at 6 to 15 month follow-up from one site in the US trial of Prodisc II. (Delamarter 2003)

      The prospective randomized study compared clinical outcomes between either anterior fusion with instrumentation and iliac crest autograft or disc replacement through an anterior retroperitoneal approach. Randomization was weighted in a 1:2 ratio. Patients were blinded to treatment until after the surgical procedure was performed.

      Disc implant involved an anterior approach with intraoperative fluoroscopy to verify placement of the disc. After a discectomy and cartilage removal from the vertebral endplates, the surgeon may have removed herniated disc material. A sagittal groove was cut in the vertebral endplates in order to accept the central keel of the implant. The final implant was impacted into place.

      Outcomes were measured with the Oswestry disability index and a pain VAS at 6 weeks, 3 months, 6 months, and 1 year. In addition, the study tracked recreational activity, ambulatory status, and medication use.

Study Population:

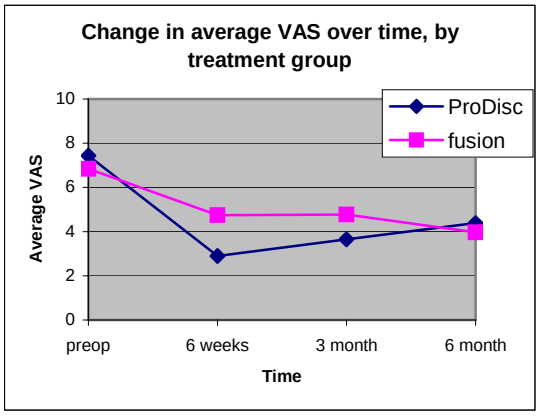
Patients were selected according to the following criteria:

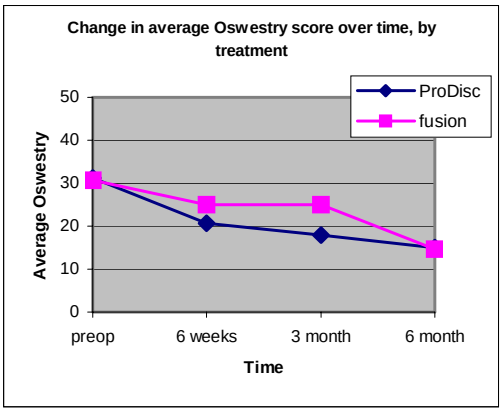
Inclusion	Exclusion
• Age 18 to 60 • Failed conservative treatment for at least 6 months • Minimum Oswestry score of 40 out of 100 • 1 or 2 level degenerative disc disease from L3 to S1	• Metal allergies • Previous lumbar fusions • Compromised vertebral bodies • Severe facet degeneration

Number of subjects by treatment group and affected levels

	ProDisc	Fusion
One level	19	8
Two level	16	10

Results: Disc replacement patients had significantly better results at 6 weeks on the VAS and 3 months on both the VAS and ODI compared to fusion patients. By 6 months, there was no significant difference between groups.





ProDisc patients experienced an increase in sagittal angular motion at 6 months for L4-L5. In contrast, fusion patients had a significant decrease in motion.

b. Zigler et al provided 6-month outcomes from the FDA trial conducted at the Texas Back Institute. (Zigler and Burd 2003)

Fusion patients were maintained in a corset for 12 weeks. At 3 months, they were referred to PT for strengthening and ROM program.

ProDisc patients were in a light corset for 2 weeks. Based on their level of function, patients underwent no formal physical therapy, a strengthening and range of motion program, or a directed program focused on strengthening the deep paraspinal muscles.

Study Population: The Zigler study included 25 patients who received the artificial disc and 11 patients who received spine fusion. One 2-level surgery patient was randomized to a fusion, and 5 underwent 2-level ProDisc surgery.

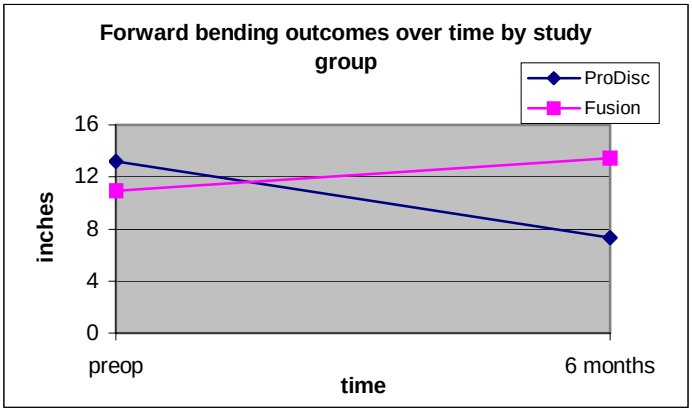
All 11 fusion patients had been symptomatic for more than 1 year, while 8 of the 28 ProDisc patients had symptom duration from 6 months to 1 year.

	ProDisc	Fusion
Only back pain	3	3
Predominately back pain with some leg pain	17	5
Back and leg pain in the same intensity	6	3
Leg pain only	2	0

Results: ProDisc patients had significantly lower operative times, blood loss, and hospital stays.

	ProDisc	Fusion
Operative time (min)	75.4	218.2
Estimated blood loss (mL)	68.9	175.0
Hospital stay (days)	2.1	3.5

At 6 weeks, 4 fusion patients had some pain at the harvest site, and 2 had some pain at 6 months.



Forward bending was measured as the distance between fingertips and floor; greater values represented more restricted the motion. The difference between groups was significant.

Oswestry scores decreased in both groups, but were only significant at 3 months favoring ProDisc. VAS also decreased for both groups, but not significantly.

The average return to full-time work for ProDisc patients was 8 weeks compared to 16 weeks for fusion patients. The 4 patients with workers' compensation claims were randomized to arthroplasty. At 6 months, none had returned to work and were on or applying for disability.

II. Published, prospective case series studies

a. Tropiano reported clinical and radiographic outcomes after an average of 1.4 years for 53 patients (mean age 45 years) who had 6 months of severe back pain and had failed non-surgical treatment. (Tropiano 2003)

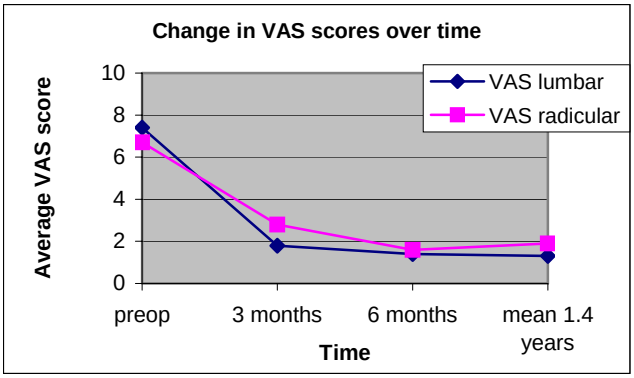
Patients were evaluated at 3 and 6 months and 1 year with a VAS and the Oswestry scale. Pain intensity was measured as excellent (1 to 2.49), good (2.5 to 4.99), fair (5 to 7.49), and poor (7.5 to 10). Evaluators were not involved in patient selection, surgery, or post-operative care.

Study Population: Preoperative diagnoses included disc degeneration (n=33) and failed spine surgery (n=20). 33 patients had not had prior surgery.

Affected levels were L5-S1 in 27 patients and L4-L5 in 13 patients. 40 patients had surgery at one level.

Results: The mean operative time was 104 minutes and mean hospital stay was 9 days.

46 patients (87%) were entirely satisfied, and 38 patients (72%) reported full resumption of work and activities. 7 workers' compensation patients stated that they could not work, but their activities were only slightly limited.



Oswestry scores improved significantly from 56% to 30% after 3 months, 18% at 6 months, and 0.14% at 1.4 years.

Outcomes did not differ between one level and multi-level patients.

b. Mayer conducted a prospective study of 34 patients (average age 44 years) examining VAS, Oswestry, and SF-36 at 3, 6, 12, and 24 months. Average follow-up was 5.8 months. (Mayer 2002)

Study Population: The study included patients with lumbar disc degeneration that failed 6 months of conservative therapy. The study also allowed patients with osteochondrosis and degeneration of levels adjacent to a former lumbar fusion.

The study excluded patients due to translational instability, spinal stenosis, osteoarthritis of the facet joints, infection, tumor, and previous fusion at the affected level.

Degenerative disc disease	61.8% (21/34)
Disc degeneration with median nucleus pulposus herniation	11.8% (4/34)
Failed back syndrome/osteochondrosis	14.7% (5/34)
Adjacent level degeneration	8.8% (3/34)
Degenerative following nucleus replacement	2.9% (1/34)

L5-S1 was affected in 24 patients, L5-L6 in 3 patients, and L4-L5 in 3 patients.

Results: 26 of 34 patients attended at least one follow-up visit.

The mean operating time was 130.9 minutes, and hospital stay averaged 12 days.

The average VAS of 6.3 decreased by 3.9 points. The average Oswestry of 19.1 points decreased by 11.5 points. 76% of patients had no low back pain at latest follow-up.

c. Bertagnoli et al conducted a case series including 134 discs replaced in 108 patients (average age 41.5 years) who failed 6 months of conservative therapy. Follow-up ranged from 3 months to 2 years. (Bertagnoli 2002)

The study measured range of motion (ROM), motor strength, Oswestry, SF-36, VAS, well being, pain sensation, and need for narcotics.

Preoperative diagnoses included:

Disc degeneration (vertical instability)	67 patients
Failed disc surgery syndrome	35 patients
Transition zone syndrome	6 patients

Results: 98 patients (90.8%) achieved excellent outcomes. However, 45 patients required analgesics for more than 2 weeks, and 12 required analgesics for a period ranging from 6 months to 1 year. 33 patients required analgesics only occasionally.

Patients resumed daily activities after an average of 2.3 weeks.

Of the 54 patients who were followed for more than 1 year, 35 patients resumed work at the same level. 17 patients resumed work at lower levels.

Disc Nucleus Replacement: PDN prosthesis

The PDN disc nucleus prosthesis addresses patients with pain by providing the cushioning function of a normal disc. The PDN is also intended to maintain disc height and flexibility.

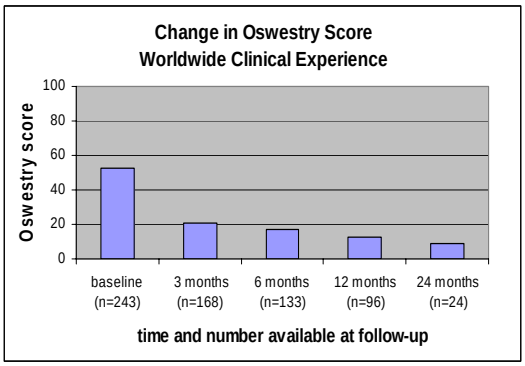
PDN is composed of a hydrogel pellet encased in a polyehtylene jacket. By absorbing 80% of its weight in water, the PDN restores or maintains disc height. In order to limit swelling, high molecular weight and linear polyethylene fibers surround the pellet. Two pellets are implanted in each enucleated disc. Pellets have platinum iridium marker wires for visualization during fluoroscopy.

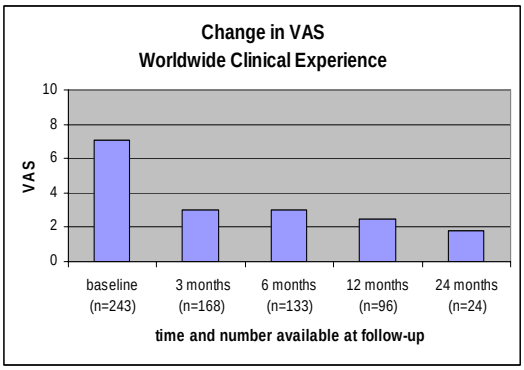
Ray, the inventor of the PDN, has suggested the following selection criteria:

- Lack of advanced disc degeneration
- Height of the central disc cavity of 5mm or greater
- Vertebral endplates free of significant defects such as Schmorl's nodules
- BMI less than 30
- Anterior posterior dimension of the affected disc large enough to accommodate the pair of devices

The PDN is implanted via a posterior hemilaminotimy approach or anterior-lateral transpsoatic approach (ALPA). First, the disc is enucleated. Small impactors are then used to drive the PDN devices through the dilated anulus. They are properly aligned transversely across the disc space. (Ray 2002)

Between 1996 and 2002, over 550 patients have been implanted with the PDN prosthetic worldwide. (Bertagnoli 2002)





I. Published Case Series Studies

a. Shim et al described outcomes for 46 patients who underwent partial disc replacement with the PDN device in a spine clinic. (Shim 2003)

VAS and Oswestry scores were measured at 6 weeks, 3 months, 6 months, and 1 year.

The surgeons used 3 different surgical approaches: posterior approach, paraspinal transforaminal approach, and anterolateral transpsoatic approach (APLA).

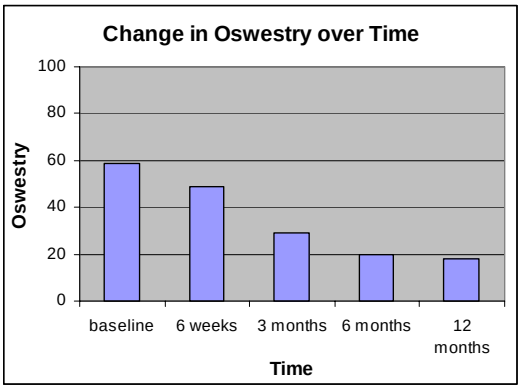
Study Population: The study included patients with chronic discogenic back pain not relieved by 6 months of conservative care. MRI indicated degeneration of the affected disc level, and a positive discogram identified the disc level.

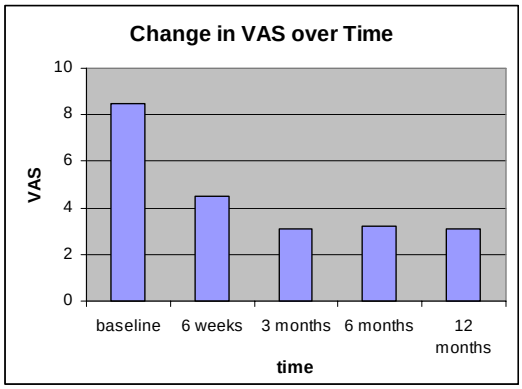
Patients were excluded due to previous disc surgery, spondylolisthesis, spinal stenosis, Schmorl nodule, osteoporosis, and disc height <5 mm.

46 patients were followed for more than 6 months, and 30 patients were followed for more than 1 year. The average age of patients was 36.5 years. 40 patients had chronic back pain and sciatica due to disc degeneration and concomitant disc herniation.

PDN was implanted at L4-L5 (n=33) and L5-S1 (n=13). 8 patients who had smaller discs received one PDN.

Results: According to MacNab criteria, 5 patients (10.9%) showed excellent results, and 31 patients (67.4%) showed good results. The clinical success rate was 78.3%.





The preoperative disc height of 10.1 mm increased by 21.3% at 6 weeks, 18.4% at 3 months, 10.9% at 6 months, and 9.4% at 12 months.

Scleroses at the endplates, like those seen in nonunion patients in interbody fusion surgery, were seen in 28 patients (60.9%). Of the 29 who underwent MRI, 24 (82.8%) showed aggravation of Modic changes of the vertebral body compared with those of the preoperative state.

b. Jin reported 6 month follow-up results of 30 patients (average age 35.6 years) with the implantation of a single PDN device. (Jin 2003)

The study measured outcomes with the Oswestry index, spinal mobility tests, and disc height.

Study population: 25 patients (83.3%) complained of back pain with sciatic radiation in one leg. The mean duration of symptoms for all patients was 12 months.

Implants occurred at the following levels: L3-L4 (n=2), L4-L5 (n=44), and L5-S1 (n=14).

Results: Mean operation time was 40 minutes while mean blood loss was 50 mL.

Oswestry scores decreased from 52.2 at baseline to 16.5 at 6 months. Mean disc height increased from 8.6 mm to 10.3 mm.

Number of patients by outcomes categories at 6 months

	Preoperative	Follow-up
Low back pain		
None	0	26
Occasional	0	4
Frequent or severe	30	0
Leg pain		
None	2	26
Occasional	2	4
Frequent or severe	26	0
Sensory disturbance		
None	5	26
Slight	10	2
Marked	5	0
Motor disturbance		
None	15	28
Slight	10	2
Marked	5	0

Conclusions

Two classes of disc replacement devices are currently available to treat degenerative disc disease through preservation and restoration of motion. Intervertebral disc prostheses address more severe degeneration, and nucleus replacement products are designed for moderate degeneration.

Among intervertebral prostheses, the FDA has approved the Charité III for marketing in the United States. The ProDisc II is awaiting approval. Among disc nucleus replacement devices, the PDN is awaiting FDA approval.

One randomized controlled trial on the Charité III was conducted as part of the FDA approval process. However, only case series data from the trial has been published. The data from one center of the multi-center trial indicated that VAS and Oswestry scores for disc replacement subjects decreased over time. While promising, the data does not indicate whether patients showed statistically significant improvement over the fusion control group.

Randomized controlled trials have been conducted to compare the ProDisc II to fusion. The Delamarter study reported that differences on VAS and Oswestry scores between study groups did not reach statistical significance at 6 months. The Zigler study showed that disc replacement subjects had decreased operation times, blood loss, and hospital stays in comparison to fusion patients. The difference between groups on forward bending was significant in favor of ProDisc patients. However, at 6 months, there were no significant differences between groups on VAS or Oswestry scores.

Case series studies have been conducted on both the Charité III and the ProDisc II. The studies all suggested that disc replacement was associated with improved outcomes. However, without a study design that included comparison groups, establishing causal effect was not possible. The case series studies were also limited by small populations. Kim and Mayer had follow-up periods of less than 6 months. Sott, Zeegers, Tropiano, and Bertagnoli did not clearly define study inclusion criteria.

Two case series studies have been conducted on the PDN nucleus replacement device. Again, causal effect was not established due to the lack of comparison groups. The Shim study suggested improved VAS and Oswestry scores as well as disc height. Jin also reported improved outcomes at 6 month follow-up. However, the 30 patients were only implanted with a single PDN device.

While disc replacement as a strategy for treating degenerative disc disease has gained substantial attention, it is not possible to draw any conclusion concerning disc replacement's effect on improving patient outcomes. As a result, disc replacement is considered investigational and controversial.

References

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